WE CLAIM:

1. A synthetic RNA catalyst capable of cleaving an RNA substrate which contains the sequence:

$$5'\text{-}F_1\text{-}CS\text{-}F_2\text{-}3',$$

wherein,

CS is a cleavage sequence; and

F_1 and F_2 each is a sequence of bases flanking the cleavage sequence;

the catalyst comprising a substrate binding portion and a "hairpin" portion, the substrate binding portion of the catalyst having the sequence:

$$3'\text{-}F_4\text{-}L_1\text{-}F_3\text{-}5'$$

wherein,

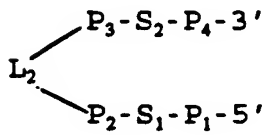
F_3 is a sequence of bases selected so that F_3 is substantially base paired with F_2 when the catalyst is bound to the substrate;

F_4 is a sequence of bases selected so that F_4 is substantially base paired with F_1 when the catalyst is bound to the substrate;

the sequences of F_3 and F_4 being selected so that each contains an adequate number of bases to achieve sufficient binding of the RNA substrate to the RNA catalyst so that cleavage of the substrate can take place; and

L_1 is a sequence of bases selected so that L_1 does not base pair with CS when the catalyst is bound to the substrate.

2. An RNA catalyst according to Claim 1, the "hairpin" portion of the catalyst having the sequence:



wherein,

P_1 and P_4 each is a sequence of bases, the sequences of P_1 and P_4 being selected so that P_1 and P_4 are substantially base paired;

P_1 is covalently linked to F_4;

S_1 and S_2 each is a sequence of bases, the sequences of S_1 and S_2 being selected so that S_1 and S_2 are substantially unpaired;

P_2 and P_3 each is a sequence of bases, the sequences of P_2 and P_3 being selected so that P_2 and P_3 are substantially base paired; and

L_2 is a sequence of unpaired bases.

3. An RNA catalyst according to Claim 1 or 2 which is capable of cleaving an RNA substrate in which CS has the sequence 5'-NGUC-3', wherein N is any base and the substrate is cleaved by the catalyst between N and G.

4. An RNA catalyst according to Claim 3 wherein L_1 has the sequence 3'-AAGA-5'.

5. An RNA catalyst according to Claim 1 or 2 wherein F_3 is at least 3 bases in length and F_4 is from 3 to 5 bases in length, and the catalyst cleaves a substrate wherein F_1 and F_2 each is at least 3 bases in length.

6. An RNA catalyst according to Claim 5 wherein F_3 is from 6 to 12 bases in length and F_4 is 4 bases in

length, and the catalyst cleaves a substrate wherein F_1 is 4 bases in length and F_2 is from 6 to 12 bases in length.

7. An RNA catalyst according to Claim 2 wherein P_1 and P_4 each is from 3 to 6 bases in length.

8. An RNA catalyst according to Claim 7 wherein P_1 has the sequence 5'-ACCAG-3' and P_4 has the sequence 5'-CUGGUA-3'.

9. An RNA catalyst according to Claim 2 wherein S_1 and S_2 each is from 4 to 9 bases in length.

10. An RNA catalyst according to Claim 9 wherein S_1 has the sequence 5'-AGAAACA-3' and S_2 has the sequence 5'-GUAUAUUAC-3'.

11. An RNA catalyst according to Claim 2 wherein P_2 and P_3 each is from 3 to 9 bases in length.

12. An RNA catalyst according to Claim 11 wherein P_2 has the sequence 5'-CAC-3' and P_3 has the sequence 5'-GUG-3'.

13. An RNA catalyst according to Claim 2 wherein L_2 is at least 3 bases in length.

14. An RNA catalyst according to Claim 13 wherein L_2 has the sequence 5'-GUU-3'.

15. An RNA catalyst according to Claim 2 wherein 5'-S_1-P_2-L_2 has the sequence 5'AGAAACACACGUU-3'.

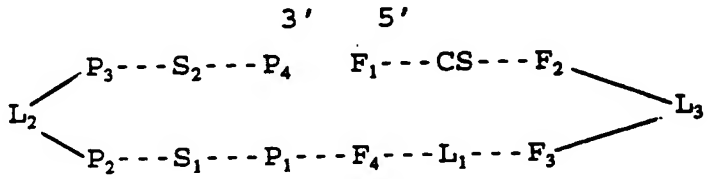
16. An RNA catalyst according to Claim 2 wherein 5'-P_2-L_2-P_3 has the sequence 5'-CACGGACUUCGGUCCGUG-3' [SEQ ID 46].

17. An RNA catalyst according to Claim 1 or 2 which is capable of cleaving an RNA substrate selected from the group consisting of messenger RNA, transfer RNA, ribosomal RNA, viral RNA, nuclear RNA, organellar RNA and other cellular RNA.

18. The catalyst of Claim 17 which is capable of cleaving an RNA substrate selected from the group consisting of HIV-1 virus RNA and tobacco mosaic virus RNA.

19. An RNA catalyst according to Claim 18 which is capable of cleaving HIV-1 RNAs containing the sequence UGCCCGUCUGUUGUGU.

20. An RNA catalyst according to Claim 2 containing the sequence:



wherein,

F_1, F_2, F_3, F_4, L_1, L_2, S_1, S_2, P_1, P_2, P_3 and P_4 are as defined in Claims 1 and 2; and

L_3 is a sequence of unpaired bases that covalently links the catalyst portion of the molecule with the substrate portion to produce a synthetic autocatalytic RNA catalyst.

21. An RNA catalyst according to Claim 20 wherein CS has the sequence 5′-NGUC-3′, wherein N is any base, and the substrate is cleaved by the catalyst between N and G.

22. An RNA catalyst according to Claim 21 wherein L_1 has the sequence 3'-AAGA-5'.

23. An RNA catalyst according to Claim 22 wherein 5'-P_1-S_1-P_2-L_2-P_3-S_2-P_4-3' has the sequence 5'-ACCAGAGAAACACACGUUGUGGUAUAUUACCUGGUA-3'.

24. An RNA catalyst according to Claim 23 wherein L_3 has the sequence 3'-CCUCC-5'.

25. A synthetic RNA catalyst which is capable of cleaving an RNA substrate containing the sequence:

5'-F_1-CS-F_2-3',

the catalyst containing the sequence:

5'-F_3-L_1-F_4-ACCAGAGAAACACACGUUGUGGUAUAUUACCUGGUA-3',

and active variants thereof,

wherein,

CS is a cleavage sequence;

F_1 and F_2 each is a sequence of bases flanking the cleavage sequence;

F_3 is a sequence of bases selected so that F_3 is substantially base paired with F_2 when the catalyst is bound to the substrate;

F_4 is a sequence of bases selected so that F_4 is substantially base paired with F_1 when the catalyst is bound to the substrate;

the sequences of F_3 and F_4 being selected so that each contains an adequate number of bases to achieve sufficient binding of the RNA substrate to the RNA catalyst so that cleavage of the substrate can take place; and

L_1 is a sequence of bases selected so that L_1 does not base pair with CS when the catalyst is bound to the substrate.

26. A synthetic RNA catalyst which is capable of cleaving an RNA substrate containing the sequence:

$$5'\text{-}F_1\text{-CS-}F_2\text{-}3',$$

the catalyst containing the sequence:

$5'\text{-}F_3\text{-}L_1\text{-}F_4$-ACCAGAGAAACACACGGACUUCGGUCCGUG-
GUAUAUUACCUGGUA-3' [SEQ ID 47]

wherein,

CS is a cleavage sequence;

F_1 and F_2 each is a sequence of bases flanking the cleavage sequence;

F_3 is a sequence of bases selected so that F_3 is substantially base paired with F_2 when the catalyst is bound to the substrate;

F_4 is a sequence of bases selected so that F_4 is substantially base paired with F_1 when the catalyst is bound to the substrate;

the sequences of F_3 and F_4 being selected so that each contains an adequate number of bases to achieve sufficient binding of the RNA substrate to the RNA catalyst so that cleavage of the substrate can take place; and

L_1 is a sequence of bases selected so that L_1 does not base pair with CS when the catalyst is bound to the substrate.

27. An RNA catalyst according to Claim 25 or 26 wherein F_3 is at least 3 bases in length and F_4 is from 3 to 5 bases in length, and the catalyst cleaves a

substrate wherein F_1 and F_2 each is at least 3 bases in length.

28. An RNA catalyst according to Claim 27 wherein F_3 is from 6 to 12 bases in length and F_4 is 4 bases in length, and the catalyst cleaves a substrate wherein F_1 is 4 bases in length and F_2 is from 6 to 12 bases in length.

29. An RNA catalyst according to Claim 25 or 26 which is capable of cleaving an RNA substrate in which CS has the sequence 5'-NGUC-3', wherein N is any base and the substrate is cleaved by the catalyst between N and G.

30. AN RNA catalyst according to Claim 29 wherein L_1 has the sequence 3'-AAGA-5'.

31. An RNA catalyst according to Claim 25 or 26 which is capable of cleaving an RNA substrate selected from the group consisting of messenger RNA, transfer RNA, ribosomal RNA, viral RNA, nuclear RNA, organellar RNA and other cellular RNA.

32. An RNA catalyst according to Claim 31 which is capable of cleaving an RNA substrate selected from the group consisting of HIV-1 virus RNA and tobacco mosaic virus RNA.

33. An RNA catalyst according to Claim 32 which is capable of cleaving HIV-1 RNAs containing the sequence UGCCCGUCUGUUGUGU.

34. An engineered DNA molecule coding for an RNA catalyst according to Claim 1, 2, 20, 25 or 26.

35. A vector comprising a DNA sequence coding for an RNA catalyst according to Claim 1, 2, 20, 25 or 26,

the DNA sequence being operatively linked to expression control sequences.

36. The vector of Claim 35 which is capable of self-replication in a host.

37. The vector of Claim 35 wherein the RNA catalyst encoded by the vector is capable of cleaving an RNA substrate selected from the group consisting of messenger RNA, transfer RNA, ribosomal RNA, viral RNA, nuclear RNA, organellar RNA and other cellular RNA.

38. The vector of Claim 37 wherein the RNA catalyst encoded by the vector is capable of cleaving an RNA substrate selected from the group consisting of HIV-1 virus RNA and tobacco mosaic virus RNA.

39. The vector of Claim 38 wherein the RNA catalyst encoded by the vector is capable of cleaving HIV-1 RNAs containing the sequence UGCCCGUCUGUUGUGU.

40. A host cell transformed with a vector according to Claim 35 and which is capable of expressing the RNA catalyst.

41. A method of cleaving an RNA substrate which contains the sequence:

$$5'F_1\text{-}CS\text{-}F_2\text{-}3',$$

wherein,

CS is a cleavage sequence; and

F_1 and F_2 each is a sequence of bases flanking the cleavage sequence;

the method comprising contacting the substrate with a synthetic RNA catalyst comprising a substrate binding portion and a "hairpin" portion, the substrate binding portion of the catalyst having the sequence:

$$3'F_4\text{-}L_1\text{-}F_3\text{-}5'$$

wherein,

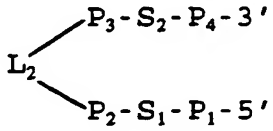
F_3 is a sequence of bases selected so that F_3 is substantially base paired with F_2 when the catalyst is bound to the substrate;

F_4 is a sequence of bases selected so that F_4 is substantially base paired with F_1 when the catalyst is bound to the substrate;

the sequences of F_3 and F_4 being selected so that each contains an adequate number of bases to achieve sufficient binding of the RNA substrate to the RNA catalyst so that cleavage of the substrate can take place; and

L_1 is a sequence of bases selected so that L_1 does not base pair with CS when the catalyst is bound to the substrate.

42. The method of Claim 41 wherein the "hairpin" portion of the catalyst has the sequence:



wherein,

P_1 and P_4 each is a sequence of bases, the sequences of P_1 and P_4 being selected so that P_1 and P_4 are substantially base paired;

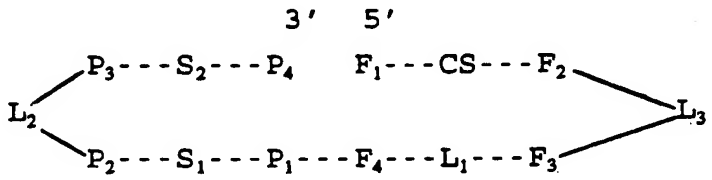
P_1 is covalently linked to F_4;

S_1 and S_2 each is a sequence of bases, the sequences of S_1 and S_2 being selected so that S_1 and S_2 are substantially unpaired;

P_2 and P_3 each is a sequence of bases, the sequences of P_2 and P_3 being selected so that P_2 and P_3 are substantially base paired; and

L_2 is a sequence of unpaired bases.

43. The method of Claim 42 wherein the catalyst has the sequence:



wherein,

F_1, F_2, F_3, F_4, L_1, L_2, S_1, S_2, P_1, P_2, P_3 and P_4 are as defined in Claims 41 and 42; and

L_3 is a sequence of unpaired bases that covalently links the catalyst portion of the molecule with the substrate portion to produce a synthetic autocatalytic RNA catalyst.

44. A method of cleaving an RNA substrate containing the sequence:

5'-F_1-CS-F_2-3',

comprising contacting the substrate with a synthetic RNA catalyst containing the sequence:

5'-F_3-L_1-F_4-ACCAGAGAAACACACGUUGUGGUAUAUUACCUGGUA-3',

and active variants thereof, wherein,

CS is a cleavage sequence;

F_1 and F_2 each is a sequence of bases flanking the cleavage sequence;

F_3 is a sequence of bases selected so that F_3 is substantially base paired with F_2 when the catalyst is bound to the substrate;

F_4 is a sequence of bases selected so that F_4 is substantially base paired with F_1 when the catalyst is bound to the substrate;

the sequences of F_3 and F_4 being selected so that each contains an adequate number of bases to achieve sufficient binding of the RNA substrate to the RNA catalyst so that cleavage of the substrate can take place; and

L_1 is a sequence of bases selected so that L_1 does not base pair with CS when the catalyst is bound to the substrate.

45. A method of cleaving an RNA substrate containing the sequence:

$$5'\text{-}F_1\text{-}CS\text{-}F_2\text{-}3',$$

comprising contacting the substrate with a synthetic RNA catalyst containing the sequence:

$5'\text{-}F_3\text{-}L_1\text{-}F_4$-ACCAGAGAAACACACGGACUUCGGUCCGUGG-
UAUAUUACCUGGUA-3' [SEQ ID 47]

wherein,

CS is a cleavage sequence;

F_1 and F_2 each is a sequence of bases flanking the cleavage sequence;

F_3 is a sequence of bases selected so that F_3 is substantially base paired with F_2 when the catalyst is bound to the substrate;

F_4 is a sequence of bases selected so that F_4 is substantially base paired with F_1 when the catalyst is bound to the substrate;

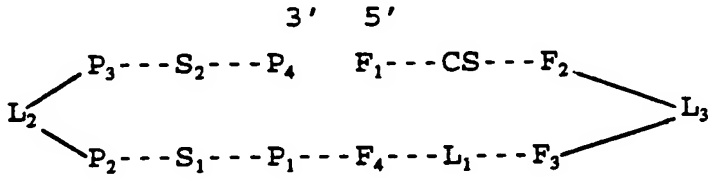
the sequences of F_3 and F_4 being selected so that each contains an adequate number of bases to achieve sufficient binding of the RNA substrate to the RNA catalyst so that cleavage of the substrate can take place; and

L_1 is a sequence of bases selected so that L_1 does not base pair with CS when the catalyst is bound to the substrate.

46. The method of Claim 41, 42, 43, 44 or 45 wherein the cleavage occurs under physiological conditions.

47. The method of Claim 46 wherein the cleavage occurs <u>in vivo</u> in a host cell which has been transformed with a vector comprising a DNA sequence coding for the RNA catalyst, the DNA sequence being operatively linked to expression control sequences.

48. A synthetic RNA transcript comprising an autocatalytic portion which has the formula:



wherein,

CS is a cleavage sequence;

F_1 and F_2 each is a sequence of bases flanking the cleavage sequence;

F_3 is a sequence of bases selected so that F_3 is substantially base paired with F_2;

F_4 is a sequence of bases selected so that F_4 is substantially base paired with F_1;

the sequences of F_3 and F_4 being selected so that each contains an adequate number of bases to achieve sufficient binding with F_1 and F_2 so that cleavage can take place;

L_1 is a sequence of bases selected so that L_1 does not base pair with CS;

P_1 and P_4 each is a sequence of bases, the sequences of P_1 and P_4 being selected so that P_1 and P_4 are substantially base paired;

S_1 and S_2 each is a sequence of bases, the sequences of S_1 and S_2 being selected so that S_1 and S_2 are substantially unpaired;

P_2 and P_3 each is a sequence of bases, the sequences of P_2 and P_3 being selected so that P_2 and P_3 are substantially base paired;

L_2 is a sequence of unpaired bases; and

L_3 is a sequence of unpaired bases.

49. A method of terminating an RNA transcript comprising:

transforming a host cell with a vector comprising DNA coding for an RNA transcript according to Claim 48;

culturing the host cell so that RNA is transcribed and the autocatalytic portion cleaves the RNA transcript to terminate the transcript.